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Attorney's Docket No.: 18202-027US1 / 1110US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : ZHI et al.
Serial No. : 10/589,920
Filed : April 20, 2007
Cust. No. : 20985
Title : GLUCOCORTICOID RECEPTOR MODULATOR COMPOUNDS AND METHODS

Art Unit : 1614
Examiner : Unknown
Conf. No. : 3750

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Request for Corrected Publication in Accordance with 37 C.F.R. §1.221(b) (5 pages), Hand-Annotated Sheets (6 pages), a copy of the Transmittal Letter dated 17 August 2006 (2 pages), a copy of the Declaration For Patent Application dated 20 April 2007 (18 pages), a copy of page 6 of the Preliminary Amendment dated 17 August 2006 (1 page), a copy of page 66 and 81 of the Supplemental Preliminary Amendment dated 18 June 2007 (2 pages), and a return postcard for filing in connection with the above-identified application.



The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 18202-027US1 / 1110US
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Stephanie Seidman



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P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CORRECTED PUBLICATION

Applicant hereby requests a Corrected Publication. The above-identified application, which Published on 12/06/2007 as Publication Number US 2007-0281959 A1, contained the following errors that were created by the USPTO:

IN THE TITLE PAGE:

In Item [75] Inventors:

In the Title Page, item [75] inventors, immediately following "Lin Zhi, San Diego CA 92130 (US)" the PTO incorrectly omitted the following inventors:

Robert J. Ardecky, Encinitas, CA 92024 (US)
Dean Phillips, San Marcos, CA 92069 (US)
John S. Tyhonas, Chula Vista, CA 91910 (US)
Donald Karanewsky, Escondido, CA 92029 (US)
Robert Higuchi, Solana Beach, CA 92079 (US)
Andrew R. Hudson, Escondido, CA 92104 (US)
Steven L. Roach, San Diego, CA 92122 (US)
Angie C. Vassar, San Diego, CA 92128 (US)
Yongkai Li, San Diego, CA 92129 (US)
Mark E. Adams, San Diego, CA 92130 (US)
Lino J. Valdez, San Diego, CA 92122 (US)
Catalina Cuervo, San Diego, CA 92117 (US)

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"Express Mail" Mailing Label Number EV 965985405 US
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I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Stephanie Seidman

Please insert the inventors listed above, such that item [75] now reads as “Lin Zhi, San Diego CA 92130 (US), Robert J. Ardecky, Encinitas, CA 92024 (US), Dean Phillips, San Marcos, CA 92069 (US), John S. Tyhonas, Chula Vista, CA 91910 (US), Donald Karanewsky, Escondido, CA 92029 (US), Robert Higuchi, Solana Beach, CA 92079 (US), Andrew R. Hudson, Escondido, CA 92104 (US), Steven L. Roach, San Diego, CA 92122 (US), Angie C. Vassar, San Diego, CA 92128 (US), Yongkai Li, San Diego, CA 92129 (US), Mark E. Adams, San Diego, CA 92130 (US), Lino J. Valdez, San Diego, CA 92122 (US), Catalina Cuervo, San Diego, CA 92117 (US).” This correction is supported in the Transmittal Letter of the national stage application, filed on 17 August 2006, and the Declaration For Patent Application, filed on 20 April 2007, which correctly lists the inventors for the above referenced application. Copies of the Transmittal Letter and the Declaration For Patent Application are provided as evidence.

IN THE CLAIMS:

On page 125 (Claim 1):

On page 125, column I, line 21 of the published application, in Claim 1, the PTO incorrectly omitted the recitation “R₁₄ and R₁₅ are each independently selected from among hydrogen, an optionally” immediately preceding the term “substituted alkyl”. Please insert the recitation “R₁₄ and R₁₅ are each independently selected from among hydrogen, an optionally” immediately preceding the term “substituted alkyl” at page 125, Column I, line 21. This correction is supported on page 6, lines 1-5 of the Preliminary Amendment, filed on 17 August 2006, which amended the claim for clarity to recite, in relevant part:

R₁₄ and R₁₅ are each independently selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted cycloalkyl and an optionally substituted heteroalkyl;

A copy of page 6 of the Preliminary Amendment of 17 August 2006 is provided as evidence.

Pursuant to MPEP 1121, the patent application publication may be based upon amendments to the claims that are reflected in a complete claim listing under 37 C.F.R. § 1.121(c), provided that such amendment is submitted in sufficient time to be entered into the Office file wrapper of the application before technical preparations for publication of the application have begun, generally four months prior to the projected date of publication. The Preliminary Amendment of 17 August 2006, which was submitted to the Office

approximately 16 months prior to the publication date of 6 December 2007 for the above referenced application, provided a complete claim listing showing amendments to the claims.

On page 126 (Claim 6):

On page 126, column II of the published application, in Claim 6, the PTO incorrectly repeated the phrase "alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl". Please delete the second recitation of "alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl" such that the claim contains a single recitation of the phrase "alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl." This correction is supported in the application as originally filed on page 280, line 20 which correctly contains a single recitation of the phrase "alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl."

On page 128 (Claim 46):

On page 128, column I of the published application, in Claim 46, the PTO incorrectly printed "R₅" instead of "R₁" in the phrase "wherein R₁ is". Please replace "R₅" with "R₁" such that Claim 46 now contains the phrase "wherein R₁ is". This correction is supported in the application as originally filed on page 285, line 6, which correctly contains "R₁" instead of "R₅" in the phrase "wherein R₁ is".

On page 134 (Claim 107):

On page 134, column II of the published application, in claim 107, the PTO incorrectly printed the term "morpholine" instead of "morpholino" in the name of compound 96. Please replace the term "morpholine" with "morpholino" such that the name of compound 96 now reads as "(Z)-5-(2'-(morpholinocarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 96);". This correction is supported on page 66, lines 1-2 of the Supplemental Preliminary Amendment, filed on 18 June 2007, which amended the claim to correct the spelling error in the name of compound 96 by replacing "morpholine" with "morpholino". A copy of page 66 of the Supplemental Preliminary Amendment of 18 June 2007 is provided as evidence.

Pursuant to MPEP 1121, the patent application publication may be based upon amendments to the claims that are reflected in a complete claim listing under 37 C.F.R. § 1.121(c), provided that such amendment is submitted in sufficient time to be entered into the Office file wrapper of the application before technical preparations for publication of the application have begun, generally four months prior to the projected date of publication. The Supplemental Preliminary Amendment of 18 June 2007, which was submitted to the Office

approximately seven months prior to the publication date of 6 December 2007 for the above referenced application, provided a complete listing of the claims.

On page 142 (Claim 108):

On page 142, column I of the published application, in claim 108, the PTO incorrectly printed the term “methylidiene” instead of “methylenidene” in the name of compound 97. Please replace the term “methylidiene” with “methylenidene” such that the name of compound 97 now reads as “(Z)-5-(8'-(6'-fluoro-benzo-1',3'-dioxan-methylenidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (compound 97);”. This correction is supported on page 81, lines 5-6 of the Supplemental Preliminary Amendment, filed on 18 June 2007, which amended the claim to correct the spelling error in the name of compound 97 by replacing “methylidiene” with “methylenidene”. A copy of page 81 of the Supplemental Preliminary Amendment of 18 June 2007 is provided as evidence.

Pursuant to MPEP 1121, the patent application publication may be based upon amendments to the claims that are reflected in a complete claim listing under 37 C.F.R. § 1.121(c), provided that such amendment is submitted in sufficient time to be entered into the Office file wrapper of the application before technical preparations for publication of the application have begun, generally four months prior to the projected date of publication. The Supplemental Preliminary Amendment of 18 June 2007, which was submitted to the Office approximately seven months prior to the publication date of 6 December 2007 for the above referenced application, provided a complete listing of the claims.

Applicant : ZHI et al.
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Request for Corrected Publication

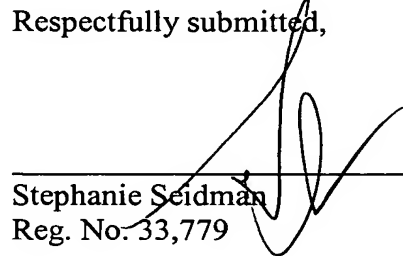
REMARKS

This Request for Corrected Publication seeks to correct typographical errors in the title page and claims introduced by the Patent and Trademark Office for publication.

Applicant respectfully requests issuance of a corrected publication.

It is believed no fee is due. However, if it is determined that a fee is due, the Office is hereby authorized to charge the fee to Deposit Account No. 06-1050.

Respectfully submitted,



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US 20070281959A1

(19) **United States**(12) **Patent Application Publication** (10) **Pub. No.: US 2007/0281959 A1**
Zhi (43) **Pub. Date: Dec. 6, 2007**(54) **GLUCOCORTICOID RECEPTOR
MODULATOR COMPOUNDS AND
METHODS**(75) **Inventor: Lin Zhi, San Diego CA 92130, CA
(US)**

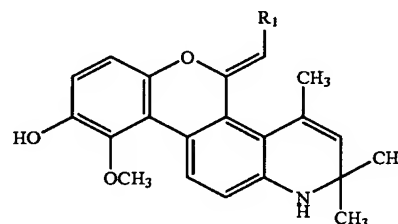
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CALIFORNIA, CA (US)**(21) **Appl. No.: 10/589,920**(22) **PCT Filed: Feb. 24, 2005**(86) **PCT No.: PCT/US05/06627**

§ 371(c)(1),
(2), (4) **Date: Apr. 20, 2007**

Related U.S. Application Data(60) **Provisional application No. 60/548,154, filed on Feb.
25, 2004.****Publication Classification**(51) **Int. Cl.**
A61K 31/4741 (2006.01)
C07D 491/02 (2006.01)(52) **U.S. Cl. 514/285; 546/62**(57) **ABSTRACT**

Disclosed herein are compounds of Formula I:



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof. Certain of such compounds are selective glucocorticoid receptor modulators and/or selective glucocorticoid binding agents. Also disclosed are methods of making and using such compounds, including, but not limited to, using such compounds for treating various conditions.

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R₁₃ is selected from among hydrogen, F, Cl, Br, CN, CONR₁₄R₁₅, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R₁₁ and R₁₂ together form an optionally substituted 5-6 member ring and R₁₃ is selected from among hydrogen, F, Cl, Br, CN, CONR₁₄R₁₅, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R₁₂ and R₁₃ together form an optionally substituted 4-6 member ring and R₁₁ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, —CONR₁₄R₁₅, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R₁₄ and R₁₅ are each independently selected from among hydrogen, an optionally

substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted cycloalkyl and an optionally substituted heteroalkyl; or

R₁₄ and R₁₅ together form an optionally substituted 4-7 member ring;

R₁₆ is selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

X is selected from among O, S, and NR₁₇; and

R₁₇ is selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl and an optionally substituted alkynyl;

wherein the substituents on the alkyl, alkenyl, alkynyl, aralkyl, aryl, heteroaryl, heterocyclyl, and cycloalkyl groups, when present, are each individually and independently selected from one to four group(s) selected from among: alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, non-aromatic heterocycle, hydroxy, alkoxy, alkoxyalkoxy, aryloxy, mercapto, alkylthio, arylthio, cyano, halo, carbonyl, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyiminothiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, trihalomethanesulfonyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylamino carbonyloxy and

amino; including mono- and di-substituted amino groups, and the protected derivatives of amino groups;

wherein at least one position selected from among R₂, R₃, R₄, R₅, and R₆ is not hydrogen;

at least one position selected from among R₇, R₈, R₉, and R₁₀ is not hydrogen;

if R₄ is F, then at least one position selected from among R₂, R₃, R₅ and R₆ is not hydrogen;

if R₃ is F, then at least one position selected from among R₂, R₄, R₅, and R₆ is not hydrogen; and

if any two positions selected from among R₂, R₃, R₄, R₅, and R₆ are both F, then at least one of the other three positions selected from R₂, R₃, R₄, R₅, and R₆ is not hydrogen.

2. The compound of claim 1, wherein R₂ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, —OR₁₆, —SR₁₆, —SO₂NR₁₄R₁₅, and an optionally substituted aryl;

R₃ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —OR₁₆, —SR₁₆ and an optionally substituted aryl; and

R₄ is selected from among hydrogen, F, Cl, Br, CN, —OR₁₆, a ring, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₂ and R₃ together form an optionally substituted 5-6 member ring and R₄ is selected from among hydrogen, F, Cl, Br, CN, —OR₁₆, a ring, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₃ and R₄ together form an optionally substituted 4-6 member ring and R₂ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, —OR₁₆, —SR₁₆, —SO₂NR₁₄R₁₅, and an optionally substituted aryl;

R₅ is selected from among hydrogen, F, Cl, Br, an optionally substituted C₁-C₄ alkyl, and OCH₃;

R₆ is selected from hydrogen and F;

R₇ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, and an optionally substituted aryl;

R₈ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —OR₁₆, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; and

R₉ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₇ and R₈ together form an optionally substituted 5-6 member ring and R₉ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₈ and R₉ together form an optionally substituted 4-6 member ring and R₇ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, and an optionally substituted aryl;

R₁₀ is selected from among hydrogen, F, Cl, CH₃, and OCH₃;

R₁₁ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, and an optionally substituted aryl;

R₁₂ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —OR₁₆, a phenyl that is optionally substituted with hydrogen, a halogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; and

R₁₃ is selected from among hydrogen, F, Cl, Br, CN, CONR₁₄R₁₅, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₁₁ and R₁₂ together form an optionally substituted 5-6 member ring and R₁₃ is selected from among hydrogen, F, Cl, Br, CN, CONR₁₄R₁₅, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₁₂ and R₁₃ together form an optionally substituted 4-6 member ring and R₁₁ is selected from among hydrogen, F, Cl, Br, CN, CONR₁₄R₁₅, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, and an optionally substituted aryl;

R₁₄ and R₁₅ are each independently selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, and an optionally substituted C₁-C₄ heteroalkyl; or

R₁₄ and R₁₅ together form an optionally substituted 4-7 member ring;

R₁₆ is selected from among hydrogen, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, and an optionally substituted aryl;

X is selected from among O, S, and NR₁₇;

R₁₇ is selected from among hydrogen and an optionally substituted C₁-C₄ alkyl; and

Wherein

at least one position selected from among R₂, R₃, R₄, R₅, and R₆ is not hydrogen;

at least one position selected from among R₇, R₈, R₉, and R₁₀ is not hydrogen;

if R₄ is F, then at least one position selected from among R₂, R₃, R₅ and R₆ is not hydrogen;

if R₃ is F, then at least one position selected from among R₂, R₄, R₅, and R₆ is not hydrogen; and

if any two positions selected from among R₂, R₃, R₄, R₅, and R₆ are both F, then at least one of the other three positions selected from among R₂, R₃, R₄, R₅, and R₆ is not hydrogen.

3. The compound of claim 1, wherein R₂ is selected from among hydrogen, halo, cyano, C₁-C₄ alkyl, C₂-C₄ alkenyl, aryl, haloalkoxy, haloalkylthio, formylaryl, hydroxyC₁-C₄alkyl, diC₁-C₄alkylaminoC₁-C₄alkyl, C₁-C₄alkylcarbonyl, hydroxyiminoC₁-C₄alkyl, alkoxyiminoC₁-C₄alkyl, alkoxyalkoxyC₁-C₄alkyl, hydroxyhaloC₂-C₄alkyl, hydroxyhaloC₂-C₄alkenyl, C₁-C₄alkylcarbonyloxyC₁-C₄alkyl, formyl, —OR₁₆, —SR₁₆, —CONR₁₄R₁₅, —SO₂NR₁₄R₁₅, wherein R₁₄ and R₁₅ are each independently selected from among hydrogen, C₁-C₄ alkyl, C₅-C₆ aryl C₁-C₄alkyl, C₃-C₇ cycloalkyl, or R₁₄ and R₁₅ together form an optionally substituted 4-7 member ring containing 1 or 2 heteroatoms selected from nitrogen and oxygen.

4. The compound of claim 1, wherein R₂ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C₁-C₄ alkyl, an optionally substituted C₁-C₄ haloalkyl, an optionally substituted C₁-C₄ heteroalkyl, —CONR₁₄R₁₅, —OR₁₆, —SR₁₆, —SO₂NR₁₄R₁₅, and an optionally substituted aryl.

5. The compound of claim 1, wherein R₂ is phenyl.

6. The compound of claim 1, wherein R₂ is selected from among hydrogen, halo, cyano, C₁-C₄ alkyl, C₂-C₄ alkenyl, haloalkoxy, hydroxyC₁-C₄alkyl, alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl, alkoxyalkoxyC₁-C₄alkyl, and hydroxyhaloC₁-C₄alkyl.

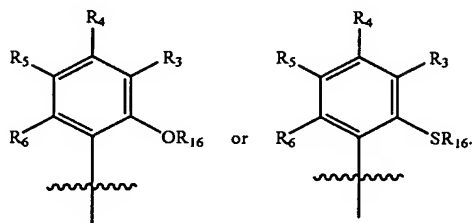
7. The compound of claim 1, wherein R₂ is selected from among hydrogen, fluoro, chloro, bromo, cyano, methyl, vinyl, hydroxymethyl, diethylaminomethyl, methoxymethoxymethyl, hydroxyiminomethyl, acetyloxymethyl, 1-hydroxy-2-trifluoroethyl, phenyl, trifluoromethoxy, trifluoromethylthio, acetyl, formyl, diethylaminocarbonyl, 3-formylphenyl, N-benzyl-N-methylaminocarbonyl, dimethylaminocarbonyl, 1-pyrrolidinocarbonyl, 1-morpholinocarbonyl, 4-methyl piperazi-1-nocarbonyl, piperidinocarbonyl, N-cyclohexyl-N-methylaminocarbonyl, piperidinosulfonyl, and N,N-dimethylaminosulfonyl.

8. The compound of claim 1, wherein R₂ is selected from among hydrogen, fluoro, chloro, cyano, methyl, hydroxymethyl, methoxymethoxymethyl, 1-hydroxy-2-trifluoroethyl, vinyl and trifluoromethoxy.

9. The compound of claim 1, wherein R₃ is selected from among hydrogen, halo, hydroxy, C₁-C₄alkoxy, C₁-C₄alkyl, haloC₁-C₄alkyl, haloalkoxy, haloC₁-C₄alkylthio, aryl, heteroaryl, haloaryloxy, aryloxy, haloaryloxy, alkoxyaryloxy, C₁-C₄alkylaryloxy, haloalkoxyaryloxy, haloaryl and hydroxyC₁-C₄alkyl.

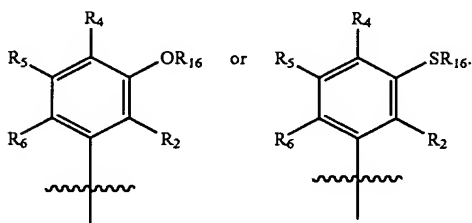
10. The compound of claim 1, wherein R₃ is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted

42. The compound of claim 1, wherein R_1 is



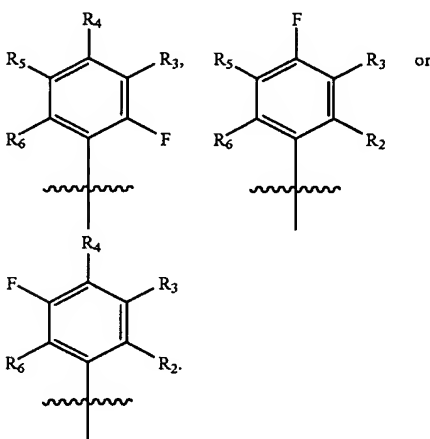
43. The compound of claim 42, wherein R_{16} is hydrogen, optionally substituted C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, optionally substituted aryl, haloaryloxy and C_1 - C_4 alkoxy C_1 - C_4 alkyl.

44. The compound of claim 1, wherein R_1 is:



45. The compound of claim 44, wherein R_{16} is hydrogen, methyl, methoxy, trifluoromethyl, 4-fluorophenyl, 4-methylbenzyl, 4,4,4-trifluorobutyl, 2-fluoroethyl, 3,3-difluoro-2,2,2-trifluoropropyl, 4-fluorobenzyl, 2-fluorobenzyl, 4-methoxyphenyl, 3,4-dichlorophenyl, 4-tolyl, 4-chlorophenyl, 3-trifluoromethoxyphenyl, and phenyl.

46. The compound of claim 1, wherein R_5 is



47. The compound of claim 1, wherein R_7 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, $-\text{CONR}_{14}\text{R}_{15}$, and an optionally substituted aryl.

48. The compound of claim 1, wherein R_7 is an optionally substituted aryl.

49. The compound of claim 1, wherein R_7 is an optionally substituted phenyl.

50. The compound of claim 49, wherein R_7 is substituted with one to three substituents selected from among hydrogen, halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, and C_1 - C_4 heteroalkyl.

51. The compound of claim 1, wherein R_7 is hydrogen.

52. The compound of claim 1, wherein R_8 is hydrogen.

53. (canceled)

54. The compound of claim 1, wherein R_9 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, and an optionally substituted C_1 - C_4 heteroalkyl.

55. The compound of claim 1, wherein R_9 is hydrogen.

56. The compound of claim 1, wherein R_7 and R_8 together form an optionally substituted 5-6 member ring and R_9 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl.

57. The compound of claim 1, wherein R_8 and R_9 together form an optionally substituted 4-6 member ring and R_7 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted C_1 - C_4 alkyl, an optionally substituted C_1 - C_4 haloalkyl, an optionally substituted C_1 - C_4 heteroalkyl, $-\text{CONR}_{14}\text{R}_{15}$, and an optionally substituted aryl.

58. The compound of claim 1, wherein R_{10} is selected from among hydrogen, F, Cl, CH_3 , and OCH_3 .

59. The compound of claim 1, wherein R_{10} is hydrogen.

60. The compound of claim 1, wherein R_{11} is selected from among hydrogen, cyano, formyl, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_2 - C_4 alkynyl, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, halo C_2 - C_4 alkenyl, hydroxy C_1 - C_4 alkyl, hydroxy C_2 - C_4 alkenyl, cyano C_1 - C_4 alkenyl, hydroxy C_2 - C_4 alkynyl, alkoxyalkoxy C_1 - C_4 alkyl, hydroxyhalo C_1 - C_4 alkyl, amino C_1 - C_4 alkyl, C_1 - C_4 alkylamino C_1 - C_4 alkyl, di C_1 - C_4 alkylamino C_1 - C_4 alkyl, C_1 - C_4 alkyl C_2 - C_4 alkenylamino C_1 - C_4 alkyl, arylamino C_1 - C_4 alkyl, C_2 - C_4 alkenylamino C_1 - C_4 alkyl, cyclo C_3 - C_6 alkylamino C_1 - C_4 alkyl, hydroxyalkoxyalkyl, haloalkylcarbonyl, alkoxyalkoxyalkoxy, carboxyalkoxyalkyl, alkoxyhaloalkyl, alkoxyalkoxyalkoxyalkyl, hydroxy C_1 - C_4 alkylcarbonyl, N,N-di C_1 - C_4 alkylamino C_1 - C_4 alkyl, N-cyclo C_3 - C_6 alkyl-N- C_1 - C_4 alkylaminocarbonyl, halo C_1 - C_4 alkylcarbonyl, hydroxyhalo C_1 - C_4 alkyl, C_1 - C_4 alkylcarbonyl, cyclo C_3 - C_6 alkylcarbonyl, C_2 - C_4 alkenylcarbonyl, C_2 - C_4 alkynylcarbonyl, heteroarylcarbonyl, hydroxyaralkyl, C_1 - C_4 alkoxy C_1 - C_4 alkyl, C_2 - C_4 alkenyloxy C_1 - C_4 alkyl, C_2 - C_4 alkynyloxy C_1 - C_4 alkyl, aryloxy C_1 - C_4 alkyl, hydroxyimino C_1 - C_4 alkyl, alkoxyimino C_1 - C_4 alkyl, C_2 - C_4 alkenyloxyimino C_1 - C_4 alkyl, aryloxyimino C_1 - C_4 alkyl, aralkoxyimino C_1 - C_4 alkyl, heterocyclyl, heteroaryl and $-\text{CONR}_{14}\text{R}_{15}$, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl groups can be unsubstituted or substituted with one to three substituents selected from among C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_2 - C_4 alkynyl, hydroxy, C_1 - C_4 alkoxy, nitro, halo, cyano, oxo, aryl, cycloalkyl, heterocyclyl, and heteroaryl groups.

61. The compound of claim 1, wherein R_{11} is selected from among hydroxy C_1 - C_4 alkyl, hydroxyimino C_1 - C_4 alkyl, C_1 - C_4 alkoxyimino C_1 - C_4 alkyl, C_1 - C_4 alkylcarbonyl, C_1 - C_4 alkenyloxyimino C_1 - C_4 alkyl, aryloxyimino C_1 - C_4 alkyl, aralkoxyimino C_1 - C_4 alkyl, C_1 - C_4 alkoxy C_1 -

- (Z)-5-(2'-Chloro-6'-fluoro-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 64);
- (Z)-5-(2'-trifluoromethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 65);
- (Z)-5-(2'-trifluoromethylthiobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 66);
- (Z)-5-(3',4'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 67);
- (Z)-5-(3'-chloro-2'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 68);
- (Z)-5-(4'-(4"-methylbenzyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 70);
- (Z)-5-(3',5'-di-tert-butylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 71);
- (Z)-5-(3'-(2",2"-difluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 72);
- (Z)-5-(2',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 73);
- (Z)-5-(3'-(3"-thienyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 74);
- (Z)-5-(2'-diethylaminocarbonylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 75);
- (Z)-5-(3'-(4",4",4"-trifluorobutoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 76);
- (Z)-5-(3'-(2",4"-difluorophenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 77);
- (Z)-5-(3'-(3"-pyridyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 78);
- (Z)-5-(2'-(3"-formylphenyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 79);
- (Z)-5-(3',5'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 80);
- (Z)-5-(3',4'-dimethylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 81);
- (Z)-5-(2'-(diethylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 82);
- (Z)-5-(2'-(diethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 83);
- (Z)-5-(2'-(methylbenzylamino)carbonyl-6'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 84);
- (Z)-5-(2'-(dimethylamino)carbonyl-5'-bromo-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 85);
- (Z)-5-(3'-(2"-fluoroethoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 86);
- (Z)-5-(3'-(2",2",3",3"-tetrafluoropropoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 87);
- (Z)-5-(3'-(4"-fluorobenzoyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 88);
- (Z)-5-(3'-(2"-fluorobenzoyloxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 89);
- (Z)-5-(2'-(pyrrolidinecarbonyl)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 90);
- (Z)-5-(2'-(pyrrolidinecarbonyl)-5'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 91);
- (Z)-5-(2'-(dimethylaminocarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 92);
- (Z)-5-(2'-(pyrrolidinecarbonyl)-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 93);
- (Z)-5-(2'-(pyrrolidinecarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 94);
- (Z)-5-(3'-(4"-fluorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 95);
- (Z)-5-(2'-(^{morpholine}carbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 96);
- (Z)-5-(8'-(6'-fluoro-benzo-1',3'-dioxan-methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 97);
- (Z)-5-(2'-(dimethylaminocarbonyl)-3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 98);
- (Z)-5-(2'-(4"-methylpiperazinecarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 99);

- (Z)-5-(2'-(pyrrolidinecarbonyl)-5'-bromobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 91);
- (Z)-5-(2'-(dimethylaminocarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 92);
- (Z)-5-(2'-(pyrrolidinecarbonyl)-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 93);
- (Z)-5-(2'-(pyrrolidinecarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 94);
- (Z)-5-(3'-(4"-fluorophenoxy)benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 95);
- (Z)-5-(2'-(morpholinocarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 96);
- (Z)-5-(8'-(6'-fluoro-benzo-1',3'-dioxan-methylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 97);
- (Z)-5-(2'-dimethylaminocarbonyl-3'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 98);
- (Z)-5-(2'-(4"-methylpiperazinecarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 99);
- (Z)-5-(2'-methyl-3'-phenylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 100);
- (Z)-5-(3',5'-di-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 101);
- (Z)-5-(2'-(piperidinecarbonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 102);
- (Z)-5-(2'-dimethylaminosulphonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 103);
- (Z)-5-(3'-phenoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 104);
- (Z)-5-(2'-(ethylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 105);
- (Z)-5-(2'-(cyclohexylmethylamino)carbonyl-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 106);
- (Z)-5-(2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 107);
- (Z)-5-(2',3',5',6'-tetrafluoro-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 108);
- (Z)-5-(3'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 109);
- (Z)-5-(2'-(piperidinesulphonyl)-4'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 110);
- (Z)-5-(1'-naphthylmethylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 111);
- (Z)-5-(3'-methyl-4'-methoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 112);
- (Z)-5-(2',5'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 113);
- (Z)-5-(2',3'-methylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 114);
- (Z)-5-(2',3'-ethylenedioxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 115);
- (Z)-5-(4'-hydroxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 116);
- (Z)-5-(2'-cyano-3'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 117);
- (Z)-5-(3'-chloro-2'-cyanobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 118);
- (Z)-5-(5'-bromo-2'-cyano-benzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 119);
- (Z)-5-(8'-(6'-chloro-benzo-1',3'-dioxan-methylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 120);
- (Z)-5-(2'-chloro-3',4'-dimethoxybenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 121);
- (Z)-5-(2'-cyano-3'-fluorobenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 122);
- (Z)-5-(8'-(6'-methyl-benzo-1',3'-dioxan-methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 123);
- (Z)-5-(2'-cyano-5'-methylbenzylidene)-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 124);
- (Z)-5-(8'-(5',6'-difluoro-benzo-1',3'-dioxan-methylidene))-1,2-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (compound 125);